G01N033-531

ICA A61K039-395; C12Q001-68

ICI C12P021-08, C12R001:19

368684 A UPAB: 19970612 AB

The following are claimed: (A) a single domain ligand comprising of at least part of the variable domain of one chain of a molecule from the immunoglobulin (Ig) superfamily; (B) a receptor comprising a ligand as in (A) linked to one or more of an effector

molecule, a prosthetic gp., a label, a solid support of other ligand(s) having the specificity; (C) a method of cloning a sequence (the target sequence) which encodes at least part of the variable domain of an

Ig superfamily molecule.

USE/ADVANTAGE - Cloning method allows for the production of monoclonal antibodies (MAbs) and bispecific antibodies and provides an alternative to hybridoma technology. The species specific primers can be used to clone pref. antibody specificity from that species without sequencing the target sequence. The ligands have equivalent binding affinity to that of complete Ig molecules and can be used in e.g. therapy (e.g. treating cancer, bacterial and viral diseases), in diagnosis, in vaccination, in modulation of activities of hormones or growth factors, in detection, in biosensors and in catalysis. The receptors can also be used in diagnosis and therapy. @(52pp Dwg.No.0/22)

FS CPI

FA

CPI: B04-B04A1; B04-B04C5; B04-B04C6; J04-B01B; J04-E MC

368684 B UPAB: 19940421 ABEQ EP

> A method of cloning sequences (target sequences) each containing a sequence encoding at least part of an immunoglobulin variable domain, which method comprises providing a sample repertoire of nucleic acid containing target sequences, and using forward and back primers in the process of copying and cloning of the target sequences for expression of a repertoire of proteins each comprising at least part of an immunoglobulin variable domain, the forward primer being specific for a sequence at or adjacent the 3' end of the sense strand of each of the target sequences, the back primer being specific for a sequence at or adjacent the 3' end of the antisense strand of each of the target sequences. Dwq.0/23

=> d his

(FILE 'HOME' ENTERED AT 13:35:48 ON 04 MAR 2004) SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:35:55 ON 04 MAR 2004

E IGG/CW

1 S E3 L1

E IGG/CT

E E3+ALL

L2 30158 S E2

57726 S IGG L3

64123 S L2, L3 L4

E A4B4L1FR

E A4B4

E S28R

L5 0 S L4 AND E3

0 S L4 AND ?S28R?

2 S L4 AND S28

rs0 S L4 AND ?A4B4? L9

0 S L4 AND ?B4L1? E DALL ACQUA W/AU

17 S E4

L10

L6

L7

```
E DALLACQUA W/AU
                E DALL A/AU
                E ACQUA/AU
              1 S E13
L11
                E JOHNSON L/AU
L12
            131 S E3
                E JOHNSON L S/AU
             16 S E3-E7
L13
                E JOHNSON LESLIE/AU
             25 S E3,E12
L14
              5 S E13-E15
L15
                E WARD E/AU
             40 S E3
L16
             77 S E23
L17
                E WARD ELIZABETH/AU
             32 S E3, E10, E11
L18
L19
              1 S E12
             29 S L4 AND L10-L19
L20
             12 S L20 AND (HALFLIVE OR HALFLIVE OR HALF()(LIFE OR LIVE))
L21
L22
            524 S L4 AND (HALFLIVE OR HALFLIVE OR HALF()(LIFE OR LIVE))
L23
             26 S L21, L22 AND ?FCRN?
                E IGG/CT
                E E33+ALL
           7702 S E2
L24
           1468 S E5
L25
L26
           3366 S E7
           14 S E9
L27
           1557 S E16
L28
           5 S E18
L29
L30
           1918 S E24
L31
           1112 S E26
L32
          71072 S L4, L24-L31
L33
            616 S L32 AND (HALFLIVE OR HALFLIVE OR HALF()(LIFE OR LIVE))
L34
             26 S L33 AND ?FCRN?
L35
             1 S L33 AND RSV
L36
            120 S L32 AND RSV
L37
              1 S L36 AND L34, L35
L38
              3 S L33 AND ROUS SARCOM? VIR?
                E RESPIRATORY SYNEC/CT
               E RESPIRATORY SYNC/CT
L39
            980 S E5
                E E5+AL
                E E3+ALL
L40
            727 S E8
L41
            980 S E7
                E E6+ALL
L42
           2278 S E7, E6+NT
L43
            179 S L32 AND L39-L42
L44
            185 S L32 AND RESPIR? SYNCYT? VIR?
L45
            120 S L32 AND RSV
L46
            191 S L43-L44
L47
              4 S L33 AND L46
L48
              1 S L34 AND L46
L49
           4918 S L32 AND (LIGHT OR HEAVY) () CHAIN
L50
            268 S L49 AND VARIAB? (L) DOMAIN
                E MUTATION/CT
L51
            732 S E3-E42 AND L32
                E E3+ALL
L52
            736 S E1+NT AND L32
                E MUTAGEN/CT
                E E5+ALL
L53
            246 S E1+NT AND L32
                E MUTAGEN/CT
```

```
L54
            185 S E5-E10 AND L32
            943 S L51-L54
L55
              8 S L55 AND L46
L56
            377 S L55 AND L49
L57
             27 S L55 AND L50
L58
L59
              8 S L55 AND ?FCRN?
L60
             17 S L22 AND L55
             94 S L20, L21, L34, L47, L48, L56, L58-L60
L61
L62
             40 S L61 AND L22
             58 S L61 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
L63
             11 S L20 NOT L63
L64
                SEL DN AN 5
L65
              1 S L64 AND E1-E3
L66
             18 S L63 AND L20
           3132 S L32 (L) (LIGHT OR HEAVY) () CHAIN
L67
             18 S L67 AND L63
L68
L69
              3 S L63 AND CONSTANT DOMAIN
L70
            194 S L32 AND CONSTANT DOMAIN
L71
             12 S L70 AND L33
L72
              2 S L70 AND L46
L73
              3 S L70 AND ?FCRN?
L74
              3 S L63 AND L70-L73
            180 S L68, L69, L70, L71 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
L75
L76
             19 S L75 AND L63
                SEL DN AN 5-7 9-13 15 18 19
              8 S L76 NOT E4-E36
L77
                SEL DN AN 6 7
              6 S L77 NOT E37-E42
L78
Ь79
              7 S L65, L78
             69 S L63, L68, L69, L71-L74 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
L80
             63 S L80 NOT L79
L81
                SEL DN AN 6 7 10 15 16 18 26 31 34 37 38 44 46
             13 S L81 AND E43-E81
L82
L83
             20 S L79, L82
L84
             22 S L20 NOT L83
             20 S L83 AND L1-L84
L85
             20 S L85 AND (IGG# OR ?IMMUNOGLOB? OR CONSTANT DOMAIN OR MUTANT? O
L86
            511 S L32 AND (TYR OR PHE OR TRP)
L87
           1823 S L32 AND (TYROS? OR PHENYLALAN? OR TRYPTOPHAN?)
L88
L89
           2196 S L87, L88
            231 S L32 AND (251 OR 252 OR 253 OR 254 OR 255 OR 256)
L90
             11 S L89 AND L90
L91
              0 S L32 AND (TYR252 OR PHE252 OR TRP252)
L92
              0 S L32 AND (TYR OR PHE OR TRP) () (251 OR 252 OR 253 OR 254 OR 255
L93
L94
             67 S L89, L90 AND L55
L95
              0 S L86 AND L87-L94
     FILE 'HCAPLUS' ENTERED AT 14:53:34 ON 04 MAR 2004
     FILE 'WPIX' ENTERED AT 14:54:43 ON 04 MAR 2004
L96
              1 S US20030190311/PN
L97
          20946 S C07K016/IC, ICM, ICS
             16 S L97 AND ?FCRN?/BIX
L98
     FILE 'MEDLINE' ENTERED AT 15:06:13 ON 04 MAR 2004
     FILE 'WPIX' ENTERED AT 15:06:43 ON 04 MAR 2004
             79 S L97 AND (RSV OR RESPIR? SYNC? VIR?)/BIX
L99
              1 S L97 AND S28R/BIX
L100
L101
              1 S L97 AND ?A4B4?/BIX
             27 S L97 AND ((251 OR 252 OR 253 OR 254 OR 255 OR 256)(L)(TYR OR T
L102
             20 S L97 AND ((251 OR 252 OR 253 OR 254 OR 255 OR 256)(S)(TYR OR T
L103
             10 S L97 AND ((251 OR 252 OR 253 OR 254 OR 255 OR 256)(20A)(TYR OR
```

L104

```
SEL DN AN 2 4
L105
             2 S E82-E85
L106
            0 S L99 AND L98
            2 S L96, L100, L101, L105
L107
            2 S L107 AND L98-L107
L108
           174 S L97 AND (HALFLIFE OR HALFLIVE OR HALF()(LIFE OR LIVE))/BIX
L109
            7 S L109 AND L98
L110
             2 S L109 AND L99
L111
             9 S L108, L110, L111
L112
              SEL DN AN 3 4 6 7 8 9
             6 S L112 AND E86-E98
L113
             3 S L112 NOT L113
L114
              E DALL ACQUA/AU
             3 S E6
L115
               E DALLACQUA/AU
               E ACQUA/AU
               E JOHNSON L/AU
           116 S E3,E21
L116
               E WARD E/AU
            24 S E3,E18
L117
           19 S L97 AND L115-L117
L118
           12 S L115-L117 AND (IGG OR IMMUNO GLOBULIN OR IMMUNOGLOBULIN)/BIX
L119
           10 S L118 NOT L119
L120
           24 S L113, L118-L120
L121
L122
          119 S L115-L117 NOT L121
            5 S L122 AND (RSV OR RESPIR? SYNC? VIR?)/BIX
L123
             2 S L122 AND PNEUMON?/BIX
L124
             6 S L122 AND RESPIR?/BIX
L125
            7 S L123-L125
L126
L127
            31 S L121, L126
```

FILE 'WPIX' ENTERED AT 15:18:55 ON 04 MAR 2004

=>

=> d his

(FILE 'HOME' ENTERED AT 13:35:48 ON 04 MAR 2004) SET COST OFF

```
FILE 'HCAPLUS' ENTERED AT 13:35:55 ON 04 MAR 2004
                E IGG/CW
L1
              1 S E3
                E IGG/CT
                E E3+ALL
L2
          30158 S E2
L3
          57726 S IGG
L4
          64123 S L2, L3
                E A4B4L1FR
                E A4B4
                E S28R
              0 S L4 AND E3
L5
L6
              0 S L4 AND ?S28R?
ь7
              2 S L4 AND S28
              0 S L4 AND ?A4B4?
L8
L9
              0 S L4 AND ?B4L1?
                E DALL ACQUA W/AU
             17 S E4
L10
                E DALLACQUA W/AU
                E DALL A/AU
                E ACQUA/AU
L11
              1 S E13
                E JOHNSON L/AU
L12
            131 S E3
                E JOHNSON L S/AU
             16 S E3-E7
L13
                E JOHNSON LESLIE/AU
             25 S E3,E12
L14
L15
              5 S E13-E15
                E WARD E/AU
             40 S E3
L16
             77 S E23
L17
                E WARD ELIZABETH/AU
             32 S E3,E10,E11
L18
L19
              1 S E12
             29 S L4 AND L10-L19
L20
             12 S L20 AND (HALFLIVE OR HALFLIVE OR HALF()(LIFE OR LIVE))
L21
            524 S L4 AND (HALFLIVE OR HALFLIVE OR HALF()(LIFE OR LIVE))
L22
             26 S L21, L22 AND ?FCRN?
L23
                E IGG/CT
                E E33+ALL
L24
           7702 S E2
           1468 S E5
L25
           3366 S E7
L26
L27
             14 S E9
L28
           1557 S E16
              5 S E18
L29
           1918 S E24
L30
L31
           1112 S E26
L32
          71072 S L4, L24-L31
L33
            616 S L32 AND (HALFLIVE OR HALFLIVE OR HALF()(LIFE OR LIVE))
L34
             26 S L33 AND ?FCRN?
L35
              1 S L33 AND RSV
            120 S L32 AND RSV
L36
              1 S L36 AND L34, L35
L37
L38
              3 S L33 AND ROUS SARCOM? VIR?
                E RESPIRATORY SYNEC/CT
                E RESPIRATORY SYNC/CT
```

```
980 S E5
L39
                E E5+AL
                E E3+ALL
            727 S E8
L40
            980 S E7
L41
                E E6+ALL
L42
           2278 S E7, E6+NT
           179 S L32 AND L39-L42
L43
L44
           185 S L32 AND RESPIR? SYNCYT? VIR?
           120 S L32 AND RSV
L45
           191 S L43-L44
L46
              4 S L33 AND L46
L47
L48
              1 S L34 AND L46
           4918 S L32 AND (LIGHT OR HEAVY) () CHAIN
L49
            268 S L49 AND VARIAB? (L) DOMAIN
L50
                E MUTATION/CT
            732 S E3-E42 AND L32
L51
                E E3+ALL
            736 S E1+NT AND L32
L52
                E MUTAGEN/CT
                E E5+ALL
            246 S E1+NT AND L32
L53
               E MUTAGEN/CT
            185 S E5-E10 AND L32
L54
            943 S L51-L54
L55
            8 S L55 AND L46
L56
            377 S L55 AND L49
L57
L58
L59
            27 S L55 AND L50
             8 S L55 AND ?FCRN?
L60
             17 S L22 AND L55
            94 S L20, L21, L34, L47, L48, L56, L58-L60
L61
            40 S L61 AND L22
L62
            58 S L61 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
L63
             11 S L20 NOT L63
L64
                SEL DN AN 5
L65
             1 S L64 AND E1-E3
             18 S L63 AND L20
L66
           3132 S L32 (L) (LIGHT OR HEAVY) () CHAIN
L67
            18 S L67 AND L63
L68
             3 S L63 AND CONSTANT DOMAIN
L69
            194 S L32 AND CONSTANT DOMAIN
L70
            12 S L70 AND L33
L71
              2 S L70 AND L46
L72
              3 S L70 AND ?FCRN?
L73
             3 S L63 AND L70-L73
L74
            180 S L68, L69, L70, L71 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
L75
             19 S L75 AND L63
L76
                SEL DN AN 5-7 9-13 15 18 19
              8 S L76 NOT E4-E36
L77
               SEL DN AN 6 7
              6 S L77 NOT E37-E42
L78
             7 S L65,L78
L79
             69 S L63, L68, L69, L71-L74 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
L80
             63 S L80 NOT L79
L81
                SEL DN AN 6 7 10 15 16 18 26 31 34 37 38 44 46
             13 S L81 AND E43-E81
L82
L83
             20 S L79, L82
             22 S L20 NOT L83
L84
             20 S L83 AND L1-L84
L85
            20 S L85 AND (IGG# OR ?IMMUNOGLOB? OR CONSTANT DOMAIN OR MUTANT? O
L86
           511 S L32 AND (TYR OR PHE OR TRP)
L87
           1823 S L32 AND (TYROS? OR PHENYLALAN? OR TRYPTOPHAN?)
L88
L89
           2196 S L87, L88
```